

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference CPW/22985	FOR FURTHER ACTION See Form PCT/PEA416	
International application No. PCT/GB2004/002906	International filing date (day/month/year) 05.07.2004	Priority date (day/month/year) 03.07.2003
International Patent Classification (IPC) or national classification and IPC C07J73/00, A61K31/58		
Applicant CIPLA LIMITED et al.		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 9 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>		
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>		
Date of submission of the demand 14.01.2005	Date of completion of this report 19.09.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Wörth, C Telephone No. +49 89 2399-8726 	

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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-7 as originally filed

Claims, Numbers

1-20 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 19 with respect to IA

because:

☒ the said international application, or the said claims Nos. 19 with respect to IA relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-12
	No: Claims	13-20
Inventive step (IS)	Yes: Claims	1-12
	No: Claims	13-20
Industrial applicability (IA)	Yes: Claims	1-18, 20
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

1. Re Item I (*Basis of the report*)

Reference is made to the following documents:

- D1: US-A-4 760 071 (RASMUSSEN GARY H ET AL) 26 July 1988 (1988-07-26)
- D2: EP-A-0 599 376 (MERCK & CO INC) 1 June 1994 (1994-06-01)
- D3: US 2002/042425 A1 (GORMLEY GLENN J ET AL) 11 April 2002 (2002-04-11)
- D4: WO 02/20553 A (REDDY M SATYANARAYANA ; RAJAN S T (IN); REKHA K SHASHI (IN); VYAS K (I) 14 March 2002 (2002-03-14)
- D5: WAWRZYCKA I ET AL: "STRUCTURAL CHARACTERIZATION OF POLYMORPHS AND MOLECULAR COMPLEXES OF FINASTERIDE" JOURNAL OF MOLECULAR STRUCTURE, ELSEVIER, AMSTERDAM, NL, vol. 474, 1999, pages 157-166, XP000920855 ISSN: 0022-2860
- D6: WO 01/32683 A (TORCAN CHEMICAL LTD ; SLEMON CLARKE (CA)) 10 May 2001 (2001-05-10)
- D7: WO 2004/039828 A (LADERAS MUNOZ MARIO ; MARTIN JUAREZ JORGE (ES); RAGACTIVES S L (ES); S) 13 May 2004 (2004-05-13)

Document D7 does not contribute prior art within the meaning of Rule 64.1(b) PCT and will not be taken into consideration for the assessment of novelty, inventive step or industrial applicability.

2. Re Item III (*Non-establishment of opinion with regard to novelty, inventive step and industrial applicability*)

Claim 19 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

3. Re Item V (*Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement*)

3.1 Subject-matter

The present international application relates to

- a process for the preparation of the known form I of finasteride (independent claims 1 and 3)
- finasteride form I obtained by the said process (independent claim 13)
- finasteride form I characterized by the level of purity (independent claims 14-16)
- pharmaceutical compositions containing finasteride form I (independent claim 17)
- the use of finasteride form I in therapy (independent claims 18 and 20)
- a method of treatment based on administration of finasteride form I (independent claim 19).

3.2 Novelty

The subject-matter of claims 1 and 3 differ from

- D1 in view of the fact that D1 is silent about finasteride of form I and does not disclose a work-up procedure according to claim 1 (see example 1a)
- D2 in view of the present feature of replacing the solvent with a non-solvent (whereas D2 discloses the addition of the non-solvent to the solvent, see ex. 3 of D2)
- D3 in view of the present feature of replacing the solvent with a non-solvent (whereas D3 discloses the addition of the non-solvent to the solvent, see ex. 1 of D3)
- D4 in view of the fact that D4 is silent about finasteride of form I and does not disclose a work-up procedure according to claim 1 (see claim 8 of D4)
- D5 in view of the fact that D5 does not disclose a process for the preparation of finasteride form I
- D6 in view of the present feature of replacing the solvent with a non-solvent (whereas D6 discloses the formation of an insoluble metal salt complex, see ex. 2 and claim 1 of D2).

Claims 2 and 4-12 are novel by consequence.

Claims 1-12 fulfill the requirements of novelty.

The subject-matter of claim 13 Claims defining a product in terms of a process is to be construed as a claim to the product as such. Accordingly, products defined in

terms of a process of manufacture are admissible only if the products as such fulfil the requirements for patentability, i.e. inter alia that they are new and inventive. A product is not rendered novel merely by the fact that it is produced by means of a new process.

Consequently, the subject-matter of claims 13 and 17-20 is anticipated by the disclosure of e.g. D2, claims 17 and 21 and example 3 and D4, example 1 and claim 1.

The subject-matter of claims 14-16 is characterized by a specific degree of purity. However, it is common general knowledge that any compound obtained by a chemical reaction normally contains impurities for various reasons. It is therefore common practice for a skilled person to further purify a compounds according to the prevailing needs and requirements. Consequently, a document disclosing a chemical compounds makes this compound available to the public in all grades of purity as desired by a person skilled in the art. Accordingly, the subject-matter of claims 14-16 is not novel in view of D2 (claims 17, 21 and example 1) and D4 (claim 1 and example 1).

The subject-matter of claims 13-20 does not fulfill the requirements of novelty.

3.3 Inventive step

Until claims have been received which satisfy Art. 33(2)PCT, a final opinion on the inventive step of the present application cannot be taken.

However, the following observations may be pointed out:

At present, documents D2 and D3 are considered as closest prior art documents. These documents disclose a process for the preparation of finasteride form I characterized by dissolving finasteride in glacial acetic acid, adding water and isolating the precipitate (see example 3 in D2 and example 1 in D3).

In view of these documents, the problem to be solved can be regarded as the provision of a further process for the preparation of finasteride form I.

The solution provided consists in a process according to present claim 1 characterised by replacing the solvent by a non-solvent.

The problem is solved in view of examples 1-3 of the present specification.

The feature "replacing the solvent by a non-solvent" of claim 1 is presently interpreted as the usual concentration of a solution of a desired product prior to the addition of a non-solvent for the purpose of crystallisation. This is a normal option a man skilled in the art would select in order to solve the problem posed without the exercise of inventive skills and does therefore not substantiate inventive step.

Accordingly, in this situation, an unexpected effect (e.g. high degree of purity) vis-à-vis the closest prior art could be considered as an indication of inventive step.

In his submission dated 27 May 2005, the Applicant provided experimental data by repeating Example 3 of D2 and Example 1 of D3 resulting in a residual solvent content of 5% (after drying 0.5%) according to the process described in the closest prior art.

Accordingly, in view of the degree of purity according to the claimed process (99.7-99.8% after drying), an unexpected effect supporting an inventive step appears to be present.

The requirements of inventive step are fulfilled for the subject-matter of claims 1-12.

3.4 Industrial applicability

For the assessment of the present claim 19 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the

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manufacture of a medicament for a new medical treatment.

4. Re Item VI (*Certain documents cited*)

Certain published documents

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (<i>valid claim</i>) (day/month/year)
WO 2004/039828	13.05.2004	29.10.2003	31.10.2002

The subject-matter of claim 1 differs from D7 in view of the present feature of replacing the solvent with a non-solvent.